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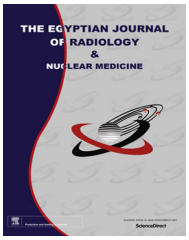

ORIGINAL ARTICLE

Predictors of positive angiography and evaluation of the outcome of transcatheter control of non variceal upper gastrointestinal hemorrhage

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KEYWORDS

Transarterial embolization;
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Abstract *Purpose:* To identify clinical factors influencing the positive angiographic findings identifying the bleeding source by angiography and to evaluation of the clinical outcome of embolization in angiography positive and in empiric embolization without identifying the bleeding source of upper gastrointestinal (UGI) bleeding.

Materials and methods: Twenty-one patients were candidates for transcatheter angiography and embolization and followed up for 3–38 months.

Results: Transcatheter angiography and embolization was technically and clinically successful in 95% and 86% respectively. Angiography identified the source in 11/20 and no source of bleeding seen in 9/20 in whom empiric embolization was carried out. Technical and clinical success or complications were not different. No procedure related major complications were encountered. Early and late mortalities were not different. Blood transfusion requirement and rate of hemoglobin drop were higher in positive compared to empiric group 9 vs 7 U and 5.7 vs 6.5 g/dL respectively ($p = 0.02$), ($p = 0.1$). Coagulopathy was found in 64% ($n = 7$) in positive and in 38% ($n = 3$) in empiric group ($p = 0.02$). Recurrent UGI bleeding was noticed in patients with coagulopathy and were treated by coils alone.

Conclusion: Transcatheter angiography and embolization is safe and effective. Embolization can be done empirically even when angiographically negative is based on endoscopic localization of bleeding source.

1. Introduction

Acute massive upper gastrointestinal (UGI) bleeding in adult is due to duodenal ulcer in about 30%-40% and gastric ulcer in 20–25%. In total, a mortality of 5%-15% has been unchanged during the last three decades often related to

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comorbidity (1). Endoscopy is the first line examination and treatment of UGI bleeding and achieves bleeding control in up to about 95% of the patients. After primary treatment failure and recurrence of bleeding, a second endoscopic attempt, surgery or endovascular embolization should be considered (2,3). When primary hemostasis has been obtained without recurrence after endoscopic treatment the mortality is less than 2%. However, in about 15% of cases endoscopy is either not available or unsuccessful (4).

Re-bleeding after primary control of bleeding is seen in about 25% of cases and these patients have mortality of about 10%. In about 5% of UGI bleeding it is not possible to stop the bleeding in the first place and in these cases the mortality is about 30% (2).

The sensitivity of angiography in detecting the bleeding source is dependent on the severity of bleeding, and is highest in hemodynamically instable patients with transfusion requirements and a bleeding of at least 1–2 mL/min before recognizing the bleeding can be expected. Further, the sensitivity is dependent on the localization of the bleeding, whether the bleeding is localized or diffused, if it is intermittent, arterial or venous, the degree of gastric and intestinal content of air, peristaltics, and patient cooperation. The sensitivity is probably no more than 50–60% (3,5,6).

Transarterial embolization (TAE) is an effective treatment with good long term results. Technical success can, in experienced hands, be achieved in 90–98% of cases (4). But about 10% will have rebleeding within 3 days (7). Primary clinical success with hemostasis in the group of patients with technically successful embolization is about 80% (4), and secondary clinical success after reembolization is achieved in more than 80% (8).

In many institutions transcatheter arterial embolization is considered as the first-line intervention for massive UGI bleeding after failed endoscopic treatment (9,10).

Many authors postulated that when the bleeding source is not identified which is considered as negative angiography and this constitutes high percentage of patients, embolization is not possible (11). Other authors concluded that: high rate of technical and clinical success was obtained with empiric transarterial embolization (TAE) comparable to identifiable TAE in patients with massive bleeding from duodenal ulcers. There were no severe complications. Empiric TAE is an effective and safe method when a bleeding site cannot be determined by angiography (12).

2. Purpose

To identify clinical factors influencing the positive angiographic findings identifying the bleeding source of nonvariceal upper gastrointestinal bleeding and to evaluation of clinical and technical outcome for transcatheter embolization of angiographically positive patient and empiric embolization of angiographically negative patient in whom angiography could not identify the bleeding source.

3. Materials and methods

This is retrospective review of all patients (n = 178) who underwent arterial embolization for acute non variceal UGI hemorrhage at a university hospital and private practice Hospital between July 2010 to October 2014. Fifteen cases were excluded because of incomplete medical records. All patients (n = 163) had an episode of massive acute bleeding within 7 days of the procedure. Patients who were presented with fresh hematemesis or circulatory instability underwent emergency endoscopy procedures by experienced endoscopists. When massive bleeding was inaccessible or unresponsive to endoscopic treatment, patients were referred for TAE, which was the first alternative to endoscopic therapy. CT angiography was obtained whenever possible, and it was not performed in patient who had renal impairment without regular dialysis and when the patient was hemodynamically unstable.

Technical success was defined as target area devascularization and clinical success was defined as clinical cessation of gastrointestinal bleeding (clearing of nasogastric aspirates and/or melena) and stabilization of the hemoglobin and hematocrit level, requiring no more than 2 units (U) of packed red blood cells after the procedure.

If a patient required more than 2 U or hemodynamic instability persist or persistent hemorrhage that required therapeutic endoscopy, repeat embolization, or surgery after the primary procedure, the procedure was considered failure.

Clinical data were obtained from the patient's medical record including: patient's age, gender, comorbidity, endoscopic diagnosis, blood transfusion requirement before and after angiography, number of blood units infused, PTT, prothrombin time and INR platelets count., rate of drop of hematocrit value per in gram per 24 h, rate of hemoglobin drop g /24 h and serum creatinine level, hospital course, and in-house mortality either hemorrhage-related mortality or for other reasons.

Coagulopathy was defined by an international normalized ratio >1.5, partial thromboplastin time >45 s, or platelet count less than 80,000 /μL. Thirty days post procedure complication can be classified as minor or major complications according to definition by SIR as an unplanned increase in the level of care, prolonged hospitalization, permanent adverse sequelae, or death. Median follow-up was 12 months ranged from 3 to 26 months average of 13 months.

3.1. Procedure

After obtaining informed consent for the procedure, diagnostic angiography through common femoral artery access with 5 Fr sheath was carried out followed by diagnostic celiac and superior mesenteric angiography. All patients then underwent selective embolization of at least one vessel, chosen by evidence of contrast extravasation at angiography which considered positive angiography or empiric embolization based on endoscopic or contrast enhanced CT before angiography. When angiography was negative, endoscopic findings were used to target embolization (empiric embolization), and the left gastric artery was chosen as the target vessel for gastric bleeding and the gastroduodenal GDA and its branches were chosen for duodenal bleeding. If subsequent angiogram demonstrated collateral flow or continued extravasation, a secondary or tertiary embolization was performed. For embolotherapy, Hilal microcoils platinum 0.18 or Tornado embolization microcoils Gelfoam pledgets or Gelfoam slurry (Pharmacia & Upjohn, Kalamazoo, MI) were deployed close to the bleeding site via superselective catheterization. Sandwich technique used coils

where 355–500-μm polyvinyl alcohol particles were sandwiched between coils.

3.2. Analysis

Bleeding recurrence, clinical success, minor complication after the procedure and early and late mortality and blood transfusion requirement after embolization were compared between positive group and empiric embolization group using Fisher exact test for univariate analysis.

4. Result

During 5 years duration, 178 patients were presented with picture of upper gastrointestinal bleeding with hematemesis and/or melena. Fifteen patients were excluded because of deficient medical record in 13 and because of lost follow-up in 2 patients.

One hundred and sixty-three patients had undergone upper endoscopy. Variceal bleeding either esophageal or gastric was found in 84 patients. Seventy-nine patients had nonvariceal upper gastrointestinal hemorrhage, and endoscopy was successful to control bleeding in 57 patients but failed in 22 patients. One patient had bleeding and duodenal perforation required prompted surgical intervention. Twenty-one patients were the study population (13 M and 8 F). Mean age was 61.2 years ranged from 46 to 83 years. The associated comorbidities were renal impairment in 6, ischemic heart disease and cardiomyopathy in 8, and respiratory failure secondary to Chronic obstructive airway disease in 4; Liver cirrhosis in 3; and Pancreatic cancer in 1 and gastric cancer in 1. Patients who have undergone angiography and embolization have been followed up for period ranged from 3 to 38 months with average of 17 months and median of 16 months.

The demographic data and associated comorbidity for patients who had positive angiography (positive group) and patients who had negative angiography and were treated by empiric embolization (called empiric group) are shown in Table 1.

Table 1 Demographic and comorbidities of patient in angiography positive and angiography negative that was treated empirically (empiric group).

	Positive group (n = 11)	Empiric group (n = 9)	P value
Age	62.6(48–72)	61.3(49–71)	0.6
M	8(72%)	6(66%)	0.3
F	3(27%)	3 (33%)	
Liver cirrhosis	2(18%)	1(11%)	
Ischemic heart and cardiomyopathy	5(45%)	3(33%)	
Respiratory failure	2(18%)	2(22%)	
Cancer	1(9%)	1(11%)	
DM	5(45%)	4 (44%)	
Renal impairment	4(36%)	2 (22%)	

DM: Diabetes Mellitus.

All of them have undergone TAE after failure of endoscopic control (n = 6), or inability to localize the bleeding area (n = 9) or recurrent bleeding after endoscopic control (n = 6).

Etiology of bleeding was duodenal ulcer (n = 7), gastric ulcer (n = 6), invasive procedure iatrogenic (n = 2), Mallory-Weiss tear (n = 3), and hemorrhagic gastritis (n = 3).

CTA was performed in 12 patients, and endoscopy could not localize exact bleeder in 9 of them and 3 in whom bleeding recurred after initial control by endoscopy.

CTA was positive with extravasations of contrast in arterial phase and increased in venus phase 33% (n = 4) (Fig. 1).

Overall technical and clinical success was 95% and 86% respectively (n = 20 and n = 18). Positive angiography with active bleeding was seen in 52% (n = 11) and empiric embolization was done in 43% (n = 9). Technical failure was encountered in single patient because of celiac trunk stenosis who was managed surgically. Devascularization of target area was obtained in 100% in both positive and empiric groups, and clinical success rates were 91% (n = 10) and 89% (n = 8) for positive and empiric groups respectively. Recurrent upper gastrointestinal bleeding was encountered in 2 patients within 7 days after embolization, one of positive group and one of empiric group. Only coils were used for embolization and both of them had coagulopathy with INR was 1.7 and 1.2, prothrombin time was 18 and 15 s and partial thromboplastin time (PTT) was 70 and 50 s respectively. The first recurrence has happened, two days after embolization of GDA by coils alone. Patient was subjected to endoscopy that showed bleeding could not be controlled endoscopically and sent for second angiography that has shown recurrent bleeding from duodenal branch from GDA. The bleeding branch was controlled by coils and PVA. Second patient had bleeding gastric ulcer that was controlled by empiric embolization of left gastric artery. Three days after embolization slow bleeding from nasogastric tube was noticed that required three units of blood transfusion over 24 h. Second endoscopy showed bleeding from gastric ulcer that was controlled endoscopically (see Table 2).

Positive angiography group of patients had significantly higher number of unit of blood transfusion prior to angiography. The median number of transfused units for those patients was 9 U of packed red blood cells (range 5–22 U), that was significantly higher than that of empiric embolization group which was 7 Units (rage 4–16) (P value 0.02).

The mean hemoglobin level for positive group and empiric group was 5.7 g/dL and 6.5 g g/dL respectively (p = 0.1). Coagulopathy was found in 64% (n = 7) in positive and in 38% (n = 3) in empiric group (p = 0.02).

Rate of HB drop was higher in positive group than in empiric group, mean 4 g/day versus 2 g/day, and mean INR for positive group was 1.8 and that of empiric group was 1.6.

There was no significant difference in comorbidity of both groups or cause of bleeding.

4.1. Embolized arteries

The patients underwent TAE of the gastroduodenal artery (GDA), anterior superior pancreaticoduodenal artery (ASPDA), or posterior superior pancreaticoduodenal artery (PSPDA), as determined by angiography or endoscopy performed before the procedure. Additional TAE was performed

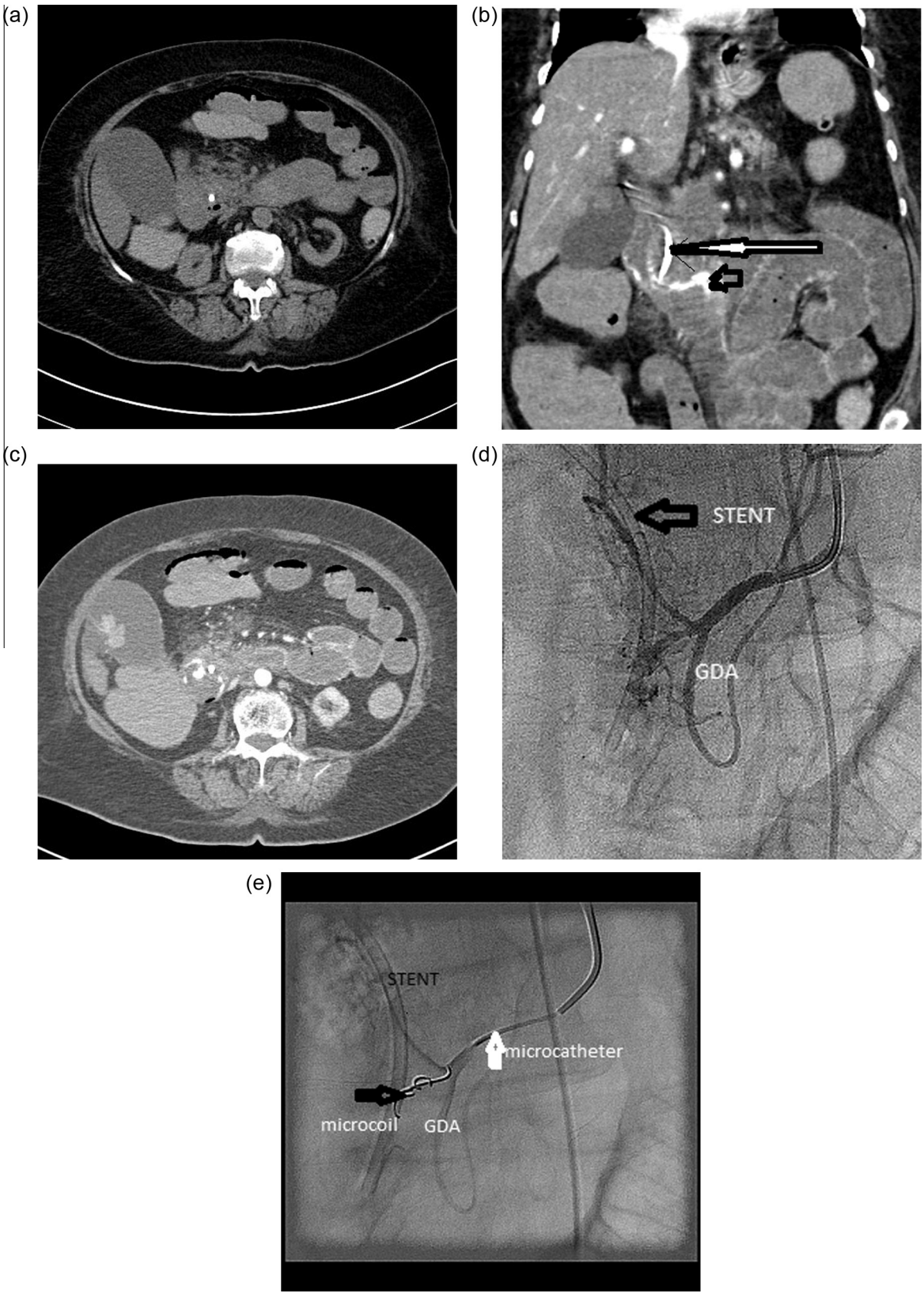

Fig. 1 (a–e) 75 years old female patient who had cancer head of pancreas and was subjected to ERCP and endoscopically-inserted biliary stent. Recently patient has presented with profuse upper gastrointestinal bleeding that could not be controlled by upper endoscopy. Noncontrast CT scan for the abdomen (a) showed the distal end of biliary stent within duodenum (thin arrow), and contrast enhanced CT (b and c) showed contrast extravasation very close to the distal end of stent (thick arrow). Transcatheter digital subtraction angiography (DSA) (d) showed contrast extravasation from the duodenal branch of gastroduodenal artery (GDA) that was embolized with tornado microcoil and PVA particles, and cessation of bleeding was noticed angiographically (e) and clinically after embolization.

Table 2 Comparison between the outcome of angiography positive and empiric groups.

	Positive $n = 11$	Empiric ($n = 9$)	P value
Recurrent bleeding	1(9%)	1(11%)	0.1
Clinical success	10(91%)	8(89%)	0.08
Complication nausea, vomiting	7(63%)	3(33%)	0.09
30 days mortality	2(18%)	1(11%)	0.1
Postembolization transfusion	1–2(1.36)	1–2(1.25)	0.19
Late mortality	2(18%)	2(22%)	0.2

in the inferior pancreaticoduodenal artery (IPDA) or dorsal pancreatic artery (DPA) if extravasation was shown via the IPDA or DPA.

When the bleeding site was the duodenal bulb, coils were deployed in the GDA as close to the hepatic artery as possible to prevent the collateral vessels supplying the duodenal bulb. If the bleeding site was the postduodenal bulb, coils were deployed in the ASPDA or PSPDA across the origin of branches feeding the bleeding site, coils were deployed in GDA close to hepatic artery in 3 and in whole GDA in 4 bleeding that were postduodenal bulb (empiric) (Fig. 2), left gastric artery in 6 (empiric in 4 and positive in 2) and in both GDA and anterior superior duodenal artery in 3 (positive) and posterior superior pancreaticodudenal artery in 2 (positive) and right gastric artery from the splenic artery in 1 (positive). Jejunal branch from SMA in one positive (Fig. 3) later showed active bleeding by technetium-tagged RBC scan.

No major procedure-related complications or mortality related to gastrointestinal bleeding was encountered in either group. Early 30 days morality was seen in 3 patients, all were not related to procedure, and all 3 patients had multiorgan

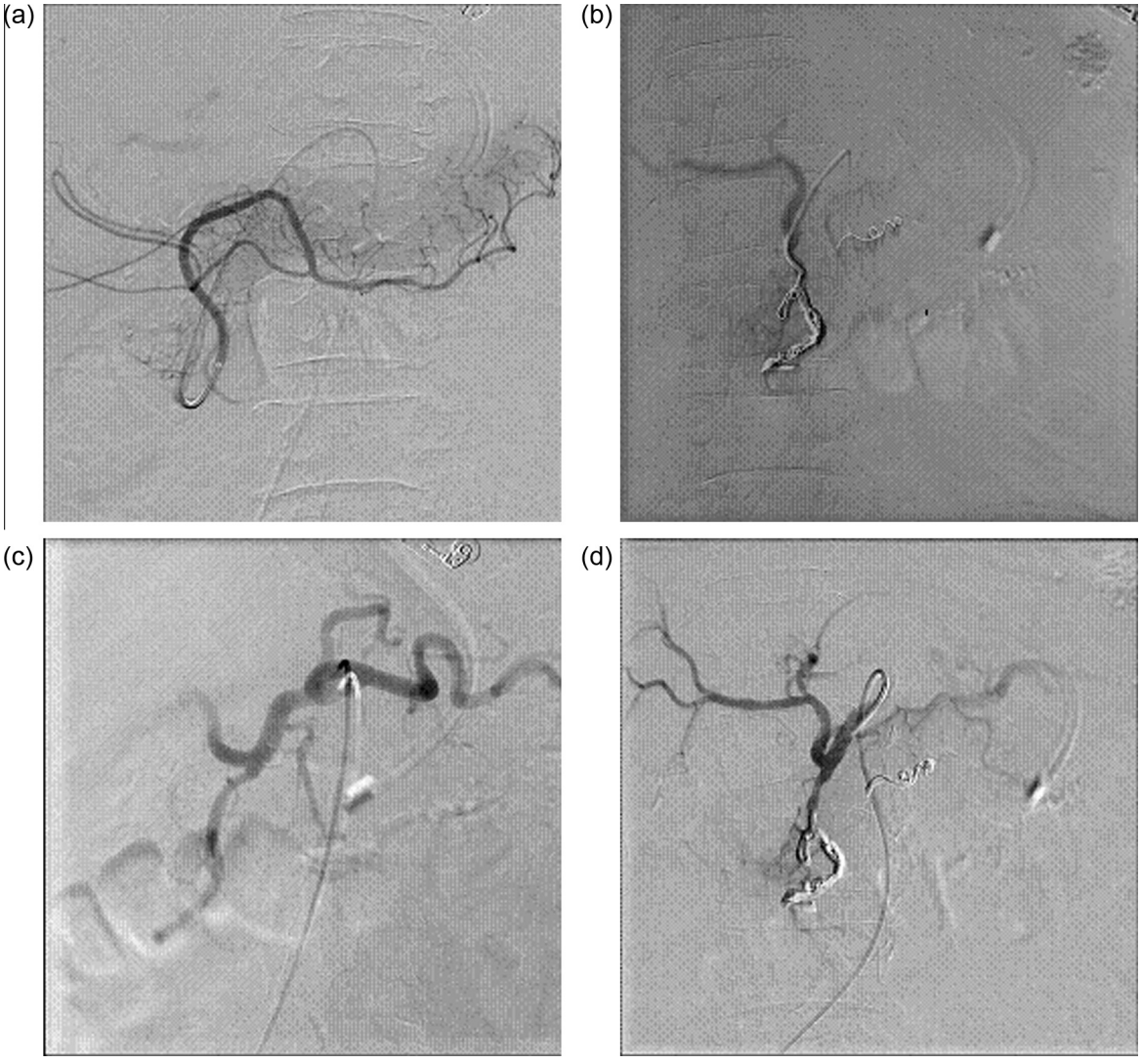

Fig. 2 (a–c) 81 years old male patient with end stage renal disease on dialysis presented with severe upper gastrointestinal bleeding from duodenal ulcer failed endoscopic treatment, and digital subtraction selective celiac (a) and SMA (b) angiography which were done revealed no active extravasation or aneurysm or other angiographic signs of active bleeding. Based on the upper GI endoscopy finding of active bleeding duodenal ulcer, empiric embolization of GDA with multiple microcoils and PVA particles was carried out. Postembolization DSA (c) showed cessation of flow at GDA. Clinically; gastrointestinal bleeding has stopped.

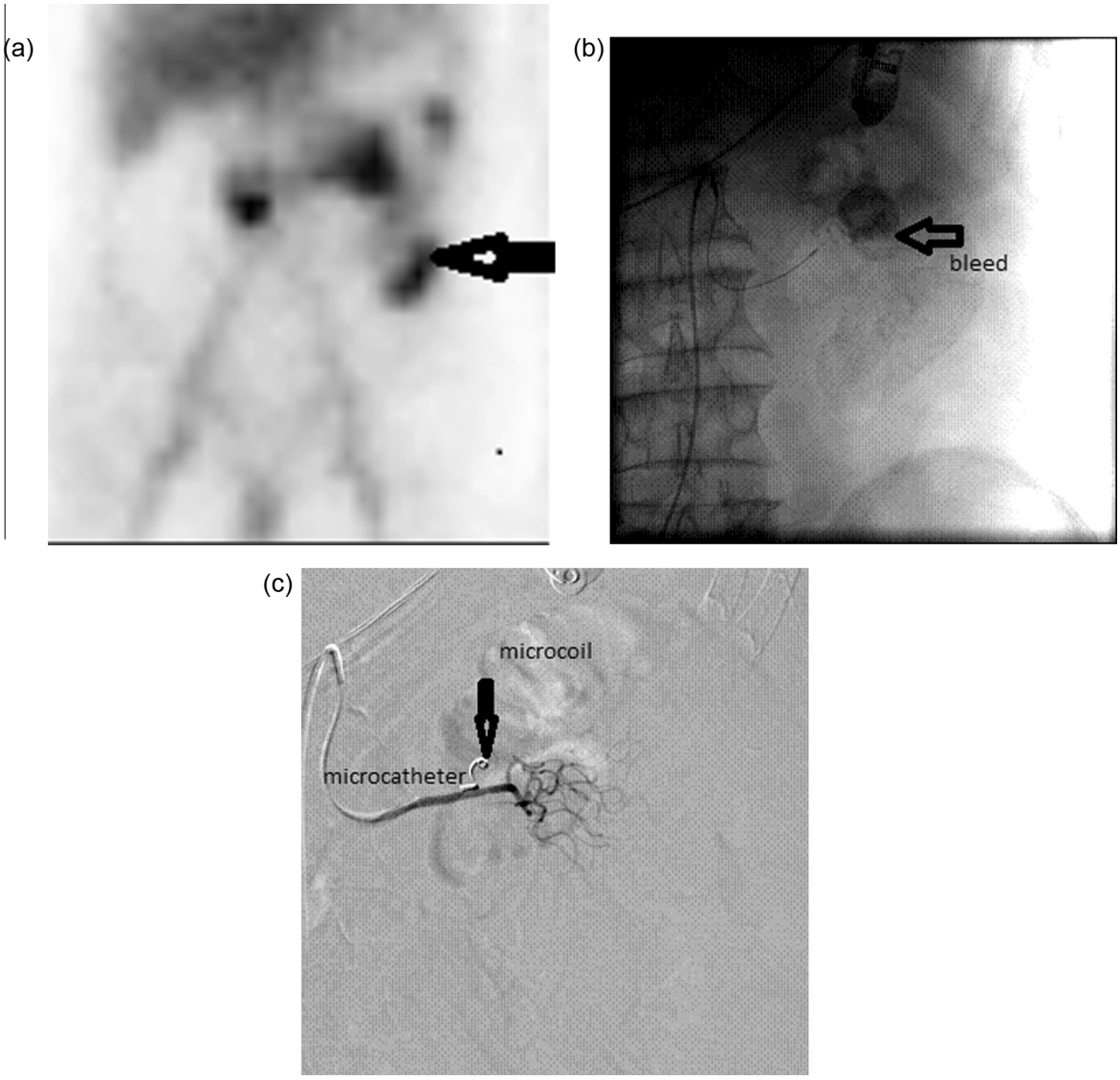

Fig. 3 (a–c) 78 years old male patient suffered from hypertension, respiratory failure, end stage renal disease was presented with intractable lower gastrointestinal bleeding, upper endoscopy was negative, autologous RBCs labeled with Tc-99m pertechnetate 18mCi were used for scanning which showed active extravasation at the left upper abdomen mostly at the proximal jejunal loop (a). DSA (b) showed the jejunal branch from SMA which showed abnormal looking distal branch with abnormal mucosal persistent staining, and super selective embolization with single microcoil has controlled the bleeding (c). Patient improved clinically without need for further blood transfusion.

failure; one suffered from liver cirrhosis and hepatorenal syndrome and one patient succumbed to respiratory failure and one patient suffered from end stag renal disease. Minor complications including nausea and vomiting in 10 cases (7 in positive and 3 in empiric) and abdominal pain in 7 (3 in positive and 4 in empiric group) all resolved by conservative treatment of antiemetic zofran and proton pump inhibitor; H1 blocker late mortalities were seen in additional 4 patients at 3, 4, 6 and 9 months after embolization first; and two patients died because of pancreatic cancer and gastric cancer. One patient deceased because of myocardial infarction and other one because of respiratory failure complicating chronic obstructive airway disease.

Postembolization blood transfusion requirement was not significantly different in both groups ranged from 1 to 2 U/24 h in positive group and 1 to 2 U/24 h in empiric group; median 1 U/24 h for both groups; and mean 1.36/24 h for positive group and 1.25 U/24 h for empiric group ($p = 0.19$).

5. Discussion

Upper endoscopy is the first line of management of upper GI Bleeding and it has been successful in 98% of cases (13). When endoscopy fails to control bleeding, the options are either surgery or transcatheter angiography and embolization. Surgery is associated with high mortality rate that ranges between 20% and 40% (14).

Transcatheter arterial embolization (TAE) has been performed for more than 30 years and has been shown to be

effective at controlling hemorrhage and decreasing mortality (15–19), with high technical and clinical success rates that are ranging from 69% to 100% and from 63% to 97% respectively (20). Therefore, currently, transcatheter embolization is considered as a good alternative to surgery for life-threatening gastroduodenal bleeding that could not be controlled by endoscopic treatment (8–10,17–19,21). When endovascular management is planned, obtaining imaging studies may be helpful. A bleeding site is often difficult to detect by angiography because massive bleeding is frequently intermittent (22). According to previous reports on endovascular management of intractable gastroduodenal bleeding, active extravasation was present in 10–100% of patients at the time of embolization (19,23,24).

Noninvasive imaging with technetium-99m-labeled red blood cell (RBC) or Tc-99m sulfur colloid scintigraphy can be used to detect and localize gastrointestinal bleeding. Tc-99m RBC scintigraphy is 93% sensitive and 95% specific for detecting a bleeding site with active arterial or venous bleeding rates as low as 0.04 mL/min (25).

Bleeding rates as low as 0.5 mL/min can be detected with selective catheter angiography (26). Angiography has a sensitivity of 63–90% for upper gastrointestinal bleeding, respectively, and a specificity of up to 100% (27,28).

An arteriogram can be obtained following a positive bleeding scan (Fig. 2), as a positive scintigram increases the likelihood of a positive angiogram from 22% to 53% (11). In our study, angiography showed extravasation in 52% of cases which is comparable to other authors who detected extravasation or pseudo aneurysm on angiography in only 39% of 59 patients (12).

In our study, positive angiography patients had criteria of massive gastrointestinal bleeding that was represented by significant higher requirement of blood transfusion and higher are of HB drop and higher percentage of coagulopathy although patients with empiric group showed lower requirement of blood transfusion and this is consistent with rapid rate of blood loss. Roughly by simple calculation requirement of 4 units or more of blood transfusion per day means the rate of blood loss at average of 0.6–1.25 ml/min which would be detectable by angiography and the lower the rate of blood loss the higher the possibility to have negative angiography results.

Bleeding, even when massive, is usually intermittent. A decrease in blood pressure secondary to massive bleeding often stops the bleeding or slows it down, making it difficult to detect (29).

Many authors postulated that when angiography is negative, which constitutes high percentage of patients, embolization is not possible (11). Other authors concluded that high rate of technical and clinical success was obtained with empiric TAE comparable to identifiable TAE in patients with massive bleeding from duodenal ulcers. There were no severe complications. Empiric TAE is an effective and safe method when a bleeding site cannot be determined by angiography (12).

In this study clinical success of embolization angiography positive active bleeding was comparable with empiric bleeding based on the endoscopy diagnosis of the source of bleeding 91% ($n = 11$) versus 89% ($n = 8$). In study of Ichiro et al. (12) the clinical success rate of positive angiography and empiric embolization of duodenal bleeding diagnosed by upper endoscopy were 86% ($n = 31$) and 78% ($n = 18$) respectively and they used Gelfoam as an embolization material but we used either coils alone or coils with PVA.

The outcome of embolization in positive and empiric groups was without significant difference as regard the clinical success and efficacy that was determined by postprocedure requirement for blood transfusion, and early and late mortality; none of them was procedure-related and also minor complications were not different in both groups.

The frequency of bleeding recurrence was comparable in both groups in whom 4 out 5 had coagulopathy and treated with coils alone and this agreed with the result of Aina et al. Loffroy et al. reported high rate of bleeding recurrence when coils only used in patienst with coagulopathy (8,9). This raises the importance of correction of coagulopathy. There has been strong correlation among coagulopathy, clinical failure, and mortality after embolization: patients with coagulopathy are 3 times more likely to experience recurrent bleeding after initially successful embolization and 10 times more likely to die as a result of bleeding compared with those with normal coagulation profile (16,8,4). Aina et al. concluded, by multivariate regression analysis, that the use of coils alone was associated with recurrent bleeding in cases with coagulopathy, a finding that supports the use of PVA or Gelfoam in combination with coils in patients with coagulopathy (8), which agreed with our successful control of early recurrent bleeding in patients with coagulopathy by the use of PVA and coils together.

Arterial phase multidetector row helical computed tomography (CT) has been reported to be accurate for detection and localization of bleeding sites in patients with acute massive GI bleeding. We used CT angiography to help localization of the source of bleeding and decrease time needed to control the bleeding (Fig. 1). Some authors do not perform CT routinely to decrease the contrast dose of the patient and avoid delay of patient for angiography (12), but on the other hand finding the source of the bleeding requires multiple superselective angiography which might be time- consuming and is associated with utilization of excessive contrast. In this study CTA was positive only in 33% of cases and this can be explained by the very short period of image acquisition in CTA and the course of bleeding that might be intermittent. Severe bleeding generates selective mesenteric hypoperfusion by producing a disproportionate mesenteric vasospasm that is mediated primarily by the renin-angiotensin axis (30).

Our study was not randomized controlled study and it had small number of patients with empiric and positive angiography. We used either coils alone or combination of coils and PVA.

This study showed that the more severe the blood loss the more likely to have positive angiography. Even when angiography was negative empiric embolization could be done safely with high clinical outcome based on endoscopy localization of upper gastrointestinal hemorrhage. The use of coils alone in patient with coagulopathy was associated with early recurrence and PVA should be used with coils. Transcatheter embolization of upper gastrointestinal bleeding was safe and effective.

Conflict of interest

We have no conflict of interest to declare.

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